Randomised, Controlled, Open Label Study of Revision of Antiretroviral Regimens from Stavudine and/or a Protease Inhibitor to Zidovudine/Lamivudine/Abacavir to Prevent or Reverse Lipodystrophy: 48-Week Data

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STUDY RATIONALE
There is a need for randomised, controlled studies with objective endpoint measures and long term follow-up to identify which combination of currently licensed ARTs is least likely to induce lipoatrophy (‘fat sparing’) and/or allow reversal of established lipoatrophy (‘fat restoration’).

We therefore studied the effects on body fat of taking antiretroviral agents associated with an increased risk of lipoatrophy (d4T and/or any PIs) compared with switching these agents to those associated with lesser risk (ZDV and ABC).

STUDY DESIGN
Open label study comparing continuation of triple regimens containing d4T or ZDV + 3TC or ddi + PI (control arm) with revision to ZDV/3TC/ABC (switch arm) in HIV-infected subjects with stable undetectable viral load (<400cps/ml for 8 weeks) and no prior ABC. Clinical lipoatrophy was not required for eligibility.

1:1 randomisation of continue or switch as follows:
- ZDV/3TC or ddI/PI — switch to ABC
- d4T/3TC or ddi/PI — switch to ABC and d4T to ZDV

Primary endpoints
Change from baseline of arm and leg fat (% and kg) on whole body DEXA scan at 24 and 48 weeks.

Secondary endpoints
1-change from baseline of intra-abdominal fat (VAT) on single cut L4 CT scan
2-fasting triglyceride, total, LDL and HDL cholesterol and venous lactate levels
3-plasma viral load

RESULTS

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<tr>
<th>VATcm</th>
<th>Total n=39</th>
<th>Baseline</th>
<th>130.55+55.17</th>
<th>24 weeks</th>
<th>138.05+55.17</th>
<th>p=0.03</th>
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<tbody>
<tr>
<td>Values on single cut L4 CT scan</td>
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<td>Values on single cut L4 CT scan</td>
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CONCLUSIONS
ZDV/3TC/ABC was associated with restoration of limb fat compared with regimens containing d4T and/or PI.

Fat restoration appeared to be greater in the arms than the legs, where it was greater after d4T+PI switch versus PI switch alone.

Fat sparing was also evident in the legs (loss of 0.011kg leg fat per month of continued d4T+PI).

Switching did not have significant effects on intra-abdominal fat or on metabolic parameters, which were normal at baseline in most study subjects.

ZDV/3TC/ABC was associated with maintenance of virological control and had no unexpected adverse effects.

REFERENCES

ABSTRACT
Background
The effects of change in antiretroviral therapy on body fat redistribution and metabolic parameters have been independently associated with higher risk of the wasting/dyslipidaemia syndrome in HIV-infected patients. We sought to evaluate whether the revision of d4T and/or PI containing regimens to ZDV/3TC/ABC would lead to safe, effective and sustained reversal of lipoatrophy and improvement in (fat sparing) and/or reversibility of fat redistribution.

Methods
A multi-centre, multi-site, open label, prospective, randomised controlled trial (RCT). Subjects selected on the basis of having stable undetectable viral load (<400cps/ml for 8 weeks) and taking one of three ART regimens containing d4T and/or PI were randomised to continue therapy or switch to ZDV/3TC/ABC, such that two universal switch regimens (ZDV/3TC/ABC) — primary endpoints included change from baseline in VAT on single cut L4 CT scan and 24-week VAT cm. Secondary endpoints were HIV/RNA, CT scan measurements, adverse events, abscess, abdominal fat in single cut L4 CT scans, anthropometric and metabolic parameters. Subjects who failed any CT scans at baseline were initially excluded from analysis, subjects who failed to have follow-up CT scans at 24 weeks were excluded from analysis, and subjects who switched from baseline CT scan studies were included in the analysis. Subjects were eligible to switch if they had stable undetectable viral load (<400 cps/ml) and had been on their current regimen for >48 weeks. Subjects who switched were followed for 48 weeks.

Results
- There was an average increase in VAT cm in the switch group (+0.73±3.1 at 24 weeks, p=0.02) compared with those who continued d4T and/or PI (+0.0±0.9 at 24 weeks, p=0.8) with a mean decrease of VAT cm in those who switched to ZDV/3TC/ABC (-0.0±0.3 at 24 weeks, p=0.02) versus those who switched to another PI-containing regimen. For metabolic parameters, there was a mean decline in LDL cholesterol in those who switched away from d4T containing regimen (-0.1±0.3 at 24 weeks, p=0.02).

Conclusions
Switching to ZDV/3TC/ABC maintained virological control and was associated with objective evidence of fat sparing in the arms and a non-sustained increase in VAT cm in the legs.

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